THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 36

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte WAYNE R. MATSON

_____

Appeal No. 1996-3409
Application 08/092,543[1]

_____

ON BRIEF

_____

Before WINTERS and WILLIAM F. SMITH, Administrative Patent Judges and McKELVEY Senior Administrative Patent Judge.

WINTERS, Administrative Patent Judge.

[1] Application for patent filed Aug. 16, 1993. According to appellant, this application is a continuation of application 07/643,541, filed Jan. 18, 1991, which is a continuation-in-part of application 07/274,505 filed Nov. 21, 1988, now U.S. patent no. 5,104,639, issued, Apr. 14, 1992, which is a divisional of application 06/797,615 filed Nov. 13, 1985, now U.S. patent no. 4,863,873, issued Sep. 5, 1989, which is a continuation of application 06/670,483 filed Nov. 13, 1984, now abandoned, which is a continuation-in-part of application 06/579,401 filed Feb. 17, 1984, now U.S. patent no. 4,511,659, issued Apr. 16, 1985, which is a continuation-in-part of application 06/472,387 filed Mar. 4, 1983, now abandoned, which is a continuation-in-part of application 06/425,183 filed Sep. 28, 1982, now abandoned, which is a continuation of application 06/111,917 filed Jan. 14, 1980, now U.S. patent no. 4,404,065, issued Sep. 13, 1983.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 20, all the claims remaining in the application.

Claims 1 and 10 are representative:

> 1. In a method for diagnosing disorders in a test individual in which fluid samples from normal unafflicted control individuals, afflicted abnormal individuals and said test individuals are analyzed to generate electrical signal patterns representative of molecular constituents of said samples, the improvement which comprises creating a data base of electrical signal patterns representative of frequency distribution of a plurality of predetermined molecular constituents of fluid samples from an epidemiologically significant number of individuals having known categories of disorders and from said unafflicted control individuals, and comparing said electrical signal patterns in said data base for conformity to electrical signal patterns representative of frequency distribution of said predetermined molecular constituents of a fluid sample from said test individual.
>
> 10. A method according to claim 1, wherein said fluid samples comprise electrochemically active compounds, and wherein each electrical signal pattern representative of frequency distribution of said plurality of predetermined constituents of said fluid samples is generated by the following steps, comprising:
>
> > passing each one of said fluid samples separately through a liquid chromatographic column for achieving time-space separation of the electrochemically active compounds of said fluid sample eluting in the column and generating electrical signals representative of the electrochemical pattern of said fluid sample using an electro-chemical detection apparatus.

The references relied on by the examiner are:

Miyagi et al. (Miyagi)	4,338,811	Jul. 13, 1982
Long et al. (Long)	4,343,767	Aug. 10, 1982
Matson (Matson '873)	4,863,873	Sep. 05, 1989
Matson (Matson '639)	5,104,639	Apr. 14, 1992

W.R. Matson, et al. (Matson 1987), "EC ARRAY SENSOR CONCEPTS AND DTA", Life Sciences, Vol. 41, pgs. 905-908 (1987).

B. Seltzer, et al. (Seltzer), "Fingerprint Pattern Differences in Early- and Late-Onset Primary Degenerative Dementia", Archives of Neurology, Vol. 43. pgs. 665-668 (1988).

C. Banissi-Sabourdy, et al. (Banissi-Sabourdy), "Electroanalytical characterization of Alzheimer's disease and ovine spongiform encephalopathy by repeated cyclic voltammetry at a capillary graphite paste electrode", J. Electroanal. Chem. vol. 343: section 28, Bioelectrochemistry and Bioenergetics, pgs. 127-147 (1992).

The claims stand rejected as follows:

I. Claims 1 through 20 under 35 U.S.C. § 112, first paragraph, as based on a specification which does not provide adequate written descriptive support for the claimed invention and does not enable any person skilled in the art to make and use the claimed invention.

II. Claims 1 through 20 under 35 U.S.C. § 112, second paragraph, as indefinite.

III. Claims 1 through 20 under 35 U.S.C. § 103 as unpatentable over Matson 1987 and Seltzer.

IV. Claims 1 through 20 under 35 U.S.C. § 103 as unpatentable over Miyagi, Long, Seltzer and the admitted state of the prior art.

V. Claims 1 through 20 under the judicially established doctrine of obviousness-type double patenting (provisional) as unpatentable over claims 1 through 20 of co-pending application serial no. 08/105,482.

VI. Claims 1, 2 and 10 under the judicially established doctrine of obviousness-type double patenting as unpatentable over claims 1 through 4 of U.S. Patent No. 4,863,873.

VII. Claims 1 through 5 and 7 through 10 under the judicially established doctrine of obviousness-type double patenting as unpatentable over claims 1, 4 through 8, 10, 12 through 16, 18, 19, 22 and 23 of U.S. Patent No. 5,104,639.

We affirm rejection V under the doctrine of obviousness-type double patenting (provisional), and reverse rejections I through IV, VI and VII.

DISCUSSION

Enablement and Written Description

The claims on appeal are directed to a method of diagnosing disorders by comparing the electrical signal pattern generated by multiple preselected constituents

in a biological sample from a test subject with a data base representative of the frequency distribution of those same constituents in samples from epidemiologically significant populations with, and without, that disorder. Some of the claims are limited to diagnosing Alzheimer's Disease or Parkinson's Disease, etc.

The rejection of claims 1 through 20 under 35 U.S.C. § 112, first paragraph, is based on the written description and enablement requirements of the statute. On inspection, however, we are unable to identify reasoning which would explain why the specification does not provide adequate written descriptive support for the claimed invention. All of the concerns raised by the examiner appear to have a bearing on whether the claims are based on an enabling disclosure.

It is well settled that the examiner bears the initial burden of providing reasons why a supporting disclosure does not enable a claim. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). If we can summarize the examiner's principal position, it is that undue experimentation would be required to practice the claimed invention because of the breadth of the claims ("the specification fails to describe in detail the protocol needed to diagnose any one of the millions of disorders encompassed by the . . . independent claim. . . . [it] would require an undue amount of experimentation and follow-up to practice the instant invention for all medical disorders

known as is encompassed by the instant claims . . ”). See the Examiner’s Answer, pages 4 and 5.

The examiner is further concerned with the absence of certain specific information (“[t]he specification fails to identify the method used to classify the samples into control and disease groups . . . [t]he specification fails to teach what level of agreement between a test individual and a particular disease is required before a classification or diagnosis of a disease state can be made”). See the Examiner’s Answer, pages 6 and 7.

The claims are indeed broad, and generating a frequency distribution data base for diseases and/or biological samples encompassed by the claims, but not demonstrated by working examples, would undoubtedly be time consuming. Nevertheless, the test for undue experimentation is not merely quantitative. As stated in PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996):

> [T]he question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation “must not be unduly extensive.” Atlas Powder Co., v. E.I. DuPont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984).

The Patent and Trademark Office Board of Appeals summarized this point in Ex parte Jackson, 217 USPQ 804, 807 (1982):

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Moreover, it is well settled that the specification need not disclose what is well known in the art. Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). The examiner has not presented evidence that those skilled in the art would be unable to identify control and disease populations from which to generate frequency distribution data bases.

We have carefully reviewed the specification, including the working examples, in light of the examiner's commentary on pages 4 through 7 and 16 through 19 of the Answer, and appellant's argument on pages 19 through 21 of the Brief and page 4 of the Reply Brief. We are persuaded that the specification provides adequate guidance enabling any person skilled in the art to generate frequency distribution databases and to diagnose disorders in addition to those of the working examples; and that the experimentation necessary to practice the full scope of the claimed invention, while considerable, would not be undue. We hold that the examiner has not set forth a reasonable basis for questioning the enablement of the claims on appeal; accordingly, the rejection of claims 1 through 20 under 35 U.S.C. § 112, first paragraph, is reversed.

Indefiniteness

All of the claims on appeal stand rejected as indefinite under 35 U.S.C. § 112, second paragraph. See the Examiner's Answer, page 7. To the extent that this rejection concerns the breadth of certain terms ("'tumors', 'carcinomas' and 'cardiovascular diseases' are indefinite since the specification gives no guidance as to what type of tumors, carcinomas and cardiovascular diseases are diagnosed by the instant method"), we are persuaded that one skilled in the art would have no difficulty in understanding the metes and bounds of these terms; and that "[b]readth is not indefiniteness." In re Gardner, 427 F.2d 786, 788, 166 USPQ 138, 140 (CCPA 1970). To the extent that this rejection concerns the lack of specific information in the claims ("[c]laim 1 is incomplete in that the level of conformity to establish a diagnosis of a particular disease state is not clearly stated"), we find that the claims are not incomplete when read in light of the specification.

The rejection of claims 1 through 20 under 35 U.S.C. § 112, second paragraph, is reversed.

Obviousness

Claims 1 through 20 stand rejected as obvious over Matson 1987 and Seltzer.

In its broadest aspect, the claimed screening method comprises comparing the electrical signal pattern generated by multiple preselected constituents in a biological sample from a test subject with a data base representative of the frequency distribution of those same constituents in samples from epidemiologically significant populations with, and without, that disorder.

Matson 1987 teaches that "[c]oulometric electrode series array sensors, coupled with liquid chromatography (n-ELC), provide a route to multiplying the resolving power of conventional [liquid chromatography] by factors of 10 to 50." The reference suggests that "[t]he use of multiple parameter assays of entire metabolic pathways is potentially a powerful tool for unraveling mechanisms of disorders . . . and classification of neurological diseases" and also describes "various techniques of multiple regression and algorithm construction" as "under investigation." See the Summary and page 908.

Seltzer discloses frequency distribution analysis of fingerprint patterns (ulner or radical loops, arches and whorls) to distinguish between early- and late-onset primary degenerative dementia.

The examiner argues that "[i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to [have] used a frequency distribution as

taught by Seltzer et al. for the classification of neurological diseases by the Matson '87 method because one of skill in the art would have recognized that as taught by Seltzer et al. the frequency distribution would have shown distinct classifiable differences between biological markers of controls and individuals with the disease." See page 8 of the Answer.

Because fingerprint patterns and metabolic profiles are distinct properties or features with no readily apparent connection, we infer that the only nexus between Matson 1987 and Seltzer is that both references are concerned with the classification of neurological disorders. We cannot agree that this alone provides the requisite reason or suggestion to combine the references in the manner proposed by the examiner.[2] A bare assertion that it would have been obvious to analyze any biological sample or parameter using any statistical model previously used to identify the presence of a neurological disorder is insufficient. Further, it is apparent from the specification that conventional mathematical/statistical models are not interchangeable in the claimed method. See the Specification, pages 17 through 19. The examiner has

[2] As stated in Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996) (citation omitted), "It is well-established that before a conclusion of obviousness may be made based on a combination of references, there must have been a reason, suggestion, or motivation to lead an inventor to combine those references."

not explained why frequency distribution probability analysis would have been selected over other models, such as linear regression analysis, stepwise regression analysis, or cluster analysis, which cannot successfully distinguish between disease and non-disease populations.

In our judgment, the reason advanced by the examiner for using frequency distribution analysis in the claimed screening method (". . . frequency distribution would have shown distinct classifiable differences . . . ") stems from appellant's description in the specification, and not from the prior art. Accordingly, the rejection of claims 1 through 20 under 35 U.S.C. § 103 as unpatentable over Matson 1987 and Seltzer is reversed.

Claims 1 through 20 also stand rejected as obvious over Miyagi, Long, Seltzer and the admitted state of the prior art.

Miyagi discloses a method of screening for disease by comparing a two-dimensional pattern diagram representing a test subject's integrated values of chromatographic peaks and retention times, with a reference data base of two-dimensional patterns generated the same way.

Long teaches that liquid chromatography, followed by electrochemical detection and analysis of the effluent, is conventional. At pages 2 through 5 of the specification,

appellant indicates that abnormalities in neurotransmitters and related substances are related to degenerative, neuropsychiatric and behavioral disorders, and that Liquid Chromatography with Electrochemical Detection (LCEC) is "a common tool for the determination of . . . metabolites in biological fluids."

Seltzer discloses frequency distribution analysis of fingerprint patterns (ulner or radical loops, arches and whorls) to distinguish between early- and late-onset primary degenerative dementia.

According to the examiner, [i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to [have] used a frequency distribution as taught by Seltzer et al. for classification of neurological diseases by the Miyagi et al. method because one of skill in the art would have recognized that as taught by Seltzer et al. the frequency distribution would have shown distinct classifiable differences between biological markers of controls and individuals with the disease. It would have been obvious to one of ordinary skill in the art to use a conventional method, such as the electrochemical analysis taught by Applicant and Long et al., for the sample fluid analysis in the process taught by Miyagi et al. so as to produce patterns which are representative of the electrochemical constituents in a body fluid which Applicant admits are known to be associated with various diseases" and "[i]t would have been

obvious to one of ordinary skill in the art to utilize a known process of analysis for detecting known constituents associated with a particular disease if one wanted to diagnose that disease." See the Examiner's Answer, the paragraph bridging pages 10 and 11.

We are not persuaded. Again, the specification teaches that mathematical/statistical models are not interchangeable in the claimed method. The examiner has not explained why frequency distribution probability analysis would have been selected over other models, such as linear regression analysis, stepwise regression analysis, or cluster analysis, which cannot successfully distinguish between disease and non-disease populations.

Again, we find no reason stemming from the prior art which would have led a person having ordinary skill to the claimed method. In our judgment, the only reason or suggestion to combine the references in the manner proposed comes from appellant's specification. Accordingly, the rejection of claims 1 through 20 as unpatentable over Miyagi, Long, Seltzer and the admitted state of the prior art is reversed.

Double Patenting

Claims 1 through 20 have been provisionally rejected under the doctrine of obviousness-type double patenting over claims 1 through 20 of copending application

serial no. 08/105,482 (‘482). The present claims are directed to “diagnosis,” while the claims of the ‘482 application are directed to “screening.” The examiner sets forth the obviousness relationship between these sets of claims, and provides tenable reasoning (Examiner’s Answer, paragraph bridging pages 11 and 12). Appellant does not counter the examiner’s reasoning, arguing only that the limitations “diagnosing disorders in a test individual,” “fluid samples,” and “predetermined molecular constituents” are not found verbatim in claim 1 of the ‘482 application and, therefore, that the instant claims “would not have been anticipated or rendered obvious by claims 1-20 of the ‘482 application.” See page 27 of the Brief. This general argument does not controvert the examiner’s position with a reasonable degree of specificity. Accordingly, we affirm the provisional rejection of claims 1 through 20 under the doctrine of obviousness-type double patenting.

Claims 1, 2 and 10 stand rejected as unpatentable over claims 1 through 4 of U.S. Patent No. 4,863,873, under the doctrine of obviousness-type double patenting; claims 1 through 5 and 7 through 10 stand rejected as unpatentable over claims 1, 4 through 8, 10, 12 through 16, 18, 19, 22 and 23 of U.S. Patent No. 5,104,639, on the same ground. None of the patented claims recites comparison with a frequency distribution database, nor is that limitation adequately addressed in either rejection.

Like the rejections under 35 U.S.C. § 103, we find no reason stemming from the patented claims which would have led a person having ordinary skill to the claimed method. The rejections of the claims on double patenting grounds over U.S. Patent Nos. 4,863,873 and 5,104,639 are reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

SHERMAN D. WINTERS Administrative Patent Judge	)
WILLIAM F. SMITH Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
FRED E. McKELVEY Senior Administrative Patent Judge	)

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